

## **REMARKS**

In the Official Action dated July 28, 2005, the amendment filed on May 16, 2005 has been entered. Claims 48 and 50-59 are pending. Claims 51-57 are objected to under 37 C.F.R. §1.75(c) for certain dependency informalities. Claims 48 and 58-59 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking descriptive support. Claims 48 and 58-59 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. Claims 48 and 58-59 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-44 of U.S. Patent No. 5,614,393. Claims 48 and 58-59 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,355,861.

This Response addresses each of the Examiner's rejections and objections. Applicant therefore respectfully submits that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

In the first instance, Applicant, through the undersigned, would like to thank the Examiner for the telephonic interview of January 12, 2006 and the follow-up telephonic communication on January 13, 2006, providing helpful suggestions for the amendments to the claims.

Claims 51-57 are objected to under 37 C.F.R. §1.75(c) for certain dependency informalities. The Examiner asserts that Claims 51-57 are in improper form because a multiple dependent claim must refer to the claims on which it depends in the alternative only.

Applicant has amended the multiple dependent claims (i.e., Claims 51, 54 and 55) to refer to the claims on which they depend, in the alternative. Applicant submits that Claims

51-57, as amended, are in proper form and in compliance with 37 C.F.R. §1.75(c). Accordingly, the objection is obviated and withdrawal thereof is therefore respectfully requested.

Claims 48 and 58-59 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking descriptive support.

The Examiner alleges that the specific structural features that are required for delta-6 desaturase activity, and thereby define the genus claimed, are not described. The Examiner alleges that Table 3 provides a listing of histidine motifs from different delta-6 desaturase genes compared to each other. The Examiner alleges that the alignments in Table 3 demonstrate that there are many differences between the sequences in the histidine motifs. Therefore, the Examiner is of the opinion that it is unclear which sequences are required for the delta-6 desaturase activity.

The Examiner's rejection is based also on certain sequence search results. The Examiner states that a search of the histidine motifs indicated that the motifs represented by SEQ ID NO: 12 and 20 are present in many other genes that do not code for delta-6 desaturases. While acknowledging that identical matches to SEQ ID NO: 6 were all delta-6 desaturases, the Examiner contends that sequences having SEQ ID NO: 6 but with only one or two amino acid substitutions include enzymes other than delta-6 desaturases. Therefore, the Examiner alleges that the recitation of the three histidine-rich motifs, and particularly any one of these motifs, is not sufficient to describe a delta-6 desaturase. In this connection, the Examiner has reconsidered the previously indicated allowability of Claim 58 in view of the large number of sequences that are allegedly homologous to the present histidine motifs. The Examiner also observes that the hybridization and wash conditions recited in Claims 58 and 59 are not highly stringent.

In the first instance, Applicant respectfully submits that the present invention is based on the isolation and identification of the first two delta-6 desaturase-encoding sequences from plants. Applicant submits that prior to the present invention, it had been recognized in the art that all membrane bound desaturases have three histidine-rich sequences (i.e., histidine-rich motifs or histidine-rich boxes). See, e.g., Okuley et al. (*The Plant Cell*, Vol. 6, 147-58, January 1994), particularly Fig 1 A, where the three histidine-rich sequences that show homology to other membrane-bound desaturases are underlined. Sperling et al. (*Prostaglandins, Leukotrienes and Essential Fatty Acids*, 68, 73-95, 2003) is a review article directed to the subject of desaturases. In Part 4, Sperling et al. highlight the structure of membrane-bound desaturases containing the three histidine-rich boxes.

Applicant respectfully submits that while borage delta-6 desaturase has all three histidine-rich boxes, which are the amino acid sequences characteristic of all desaturases, the present invention identifies that the three histidine-rich boxes from borage or other plant species have distinct sequences. See the specification, particularly in Example 9 starting at page 38 and Table 3 on page 40. In this regard, Applicant submits that the Examiner improperly relies on Table 3 to allege the lack of descriptive support. Applicant submits that contrary to the Examiner's allegation, Table 3 is not a comparison of "different delta-6 desaturases." Indeed, Table 3 compares three histidine motifs of certain membrane bound desaturases and demonstrates that plant delta-6 desaturases, e.g., Borage delta-6 desaturase, have distinct specific structural features (histidine-rich motifs). Thus, the present invention recognizes that the three histidine-rich motifs of plant delta-6 desaturases are distinct from the corresponding motifs that are conserved in all other member-bound desaturases, e.g., delta-12 and delta-15 desaturases or delta-6 desaturases in species other than plants.

In addition, Applicant submits that the identification of another plant delta-6 desaturase from evening primrose is a further indication to one skilled in the art that the inventor was in possession of all plant delta-6 desaturases at the time the application was filed. The specification discloses that delta-6 desaturase from evening primrose has virtually the same histidine-rich motifs as those from Borage, which are distinct from the corresponding histidine-rich motifs in all other desaturases. Applicant respectfully submits that the case law only requires a disclosure of "a representative number" of species and does not hold that two species is not a representative number. In fact, the three histidine-rich motifs in six other plant delta-6 desaturases later identified are virtually identical to those from Borage or evening primrose. See Exhibits 1-7 filed together with our previous response. Exhibits 1-7 further corroborate that the present inventor had possession of the present invention in its full scope at the time the application was filed.

However, in an effort to favorably advance the prosecution, Applicant has also amended the claims and added a new Claim 60. Claims 48, as amended, and newly added Claim 60 further delineates the claimed plant delta-6 desaturases to comprise all three histidine-rich motifs. Claim 59, as amended, recites "hybridizing . . . molecule encoding . . . SEQ ID NO: 6, SEQ ID NO: 12 and SEQ ID NO: 20." Support for the amendments to the claims and the newly added Claims can be found throughout the specification, e.g., bottom of page 48, Examples 9 and 15 and Table 3. No new matter is introduced.

With respect to the Examiner's sequence search results, Applicant submits that the mere fact that there are the numerous motifs identical, or highly homologous, to SEQ ID NOs: 6, 12 or 20, in certain other enzymes, without more, is irrelevant to the present invention. The Examiner does not allege, nor can the Examiner provide any evidence that these enzymes other

than plant delta-6 desaturases have all three histidine-rich motifs, which are well recognized and defined in the art.

Accordingly, Applicant respectfully submits that the specification discloses sufficiently detailed and relevant identifying specific structural features of the claimed molecules, e.g., the function of the encoded protein as a plant delta-6 desaturase (determined by an enzymatic assay as disclosed), the three histidine- rich boxes, and the hybridization features. Those skilled in the art would understand that Applicant had possession of a DNA encoding a plant delta-6 desaturase at the time the application was filed. Thus, Applicant respectfully submits that the present application fully complies with the written description requirement under 35 U.S.C. § 112, first paragraph.

In view of the foregoing, Applicant respectfully submits that the rejection of Claims 48 and 58-59 under 35 U.S.C. §112, first paragraph, is overcome. Applicant respectfully requests that the Examiner withdraw the rejection based on the written description requirement of 35 U.S.C. § 112, first paragraph.

Claims 48 and 58-59 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. The Examiner acknowledges that the specification enables isolated nucleic acid sequences that encode a delta-6 desaturase from the plant species: evening primrose and borage, and from Synechocystis and cyanobacteria. However, the Examiner alleges that the specification does not provide enablement for any delta-6 desaturase from any species. The Examiner alleges that it would require undue experimentation to make and/or use the invention as broadly claimed for the reasons of record in the last office action.

Applicant respectfully submits that Claims 48 and 58-59, as amended, do not recite any delta-6 desaturase from any species. Rather, Claims 48 and 58-59 are directed to plant

delta-6 desaturase. Additionally, Applicant in the present response further delineates the claimed plant delta-6 desaturase to include all three histidine-rich motifs and the specific sequences to identify such motifs.

Applicant submits that based on the teaching in the specification, those skilled in the art would be able to identify a plant delta delta-6 desaturase gene, as presently claimed, without undue experimentation. In this regard, Applicant respectfully submits that both the assay for determining the enzymatic activity of delta-6 desaturases, and hybridization techniques, are routine in the art. The structural features, i.e., the histidine-rich boxes, certainly also facilitate the identification of a gene as coding for a delta-6 desaturase.

As evidence that the identification of additional plant delta-6 desaturases genes would not be undue, Applicant respectfully directs the Examiner's attention to the publications submitted in the previous response: Sperling et al., *Eur. J. Biochem.*, 267:3801-3811 (2000), Girke et al., *The Plant Journal*, 15:39-48 (1998) and Garcia-Maroto, *Lipids*, 37:417-426 (2002).

In Sperling et al., the delta-6 desaturase from the plant, *Ceratodon purpureus*, was identified and characterized using primers derived from the sequences encoding or surrounding histidine-rich domains and a yeast gain-of-function assay.

In Girke et al., the delta-6 desaturase cDNA of *Physcomitrella patens* was identified using primers derived from sequences encoding or surrounding similar histidine-rich motifs, and a function assay that included the profiling of fatty acids by gas liquid chromatography.

In Garcia-Maroto, the genes encoding the delta-6 desaturase of two plants, *Echium gentianoides* and *Echium pitardii*, were identified and characterized using primers derived from sequences encoding or surrounding similar histidine-rich motifs.

In view of the foregoing, Applicant respectfully submits that those skilled in the art would be able to isolate a plant delta-6 desaturase gene, as presently claimed, without undue experimentation. Accordingly, the rejection of Claims 48 and 58-59 under 35 U.S.C. §112, first paragraph, is overcome. Applicant respectfully requests the withdrawal of the rejection based on the enablement requirement.

Claims 48 and 58-59 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-44 of U.S. Patent No. 5,614,393. Claims 48 and 58-59 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,355,861. The Examiner acknowledges that the conflicting claims are not identical. However, the Examiner alleges that the conflicting claims are not patentably distinct from each other because the present claims in each of the cited patents are obvious over the patented claims.

In an effort to favorably advance the prosecution, Applicant has enclosed a Terminal Disclaimer, which states that the term of a patent issued in the present application will be co-terminus with U.S. Patent No. 5,614,393 or U.S. Patent No. 6,355,861, whichever expires earlier.

Accordingly, the rejection of Claims 48 and 58-59 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-44 of U.S. Patent No. 5,614,393 or claims 1-40 of U.S. Patent No. 6,355,861 is overcome. Therefore, withdrawal thereof is respectfully requested.

In view of foregoing amendments and remarks, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Frank S. DiGiglio', with a stylized flourish at the end.

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